REMARKS/ARGUMENTS

A. **General:**

1. Claim 16 has been amended.
2. Claims 1-47 remain in the application.

B. **Claim Objections:**

The Examiner has objected to claims 16 and 23 because of informalities.

Applicant has amended claim 16 to depend from claim 14 thereby obviating this rejection as to it. The Examiner states that claim 23 is identical to claim 1; however, claim 23, line 12, recites that the third array is a delta interval representative of the difference between non-successive elements of the second array whereas in claim 1 this difference is between successive elements of the second array so the two claims are not identical and no correction should be required.

C. **§103 Rejection:**

This Examiner has rejected claims 1-47 under 35 USC 103 (a) as being unpatentable over Meyer (US Patent No. 6,308,098) in view of Sun et al. (US Patent No. 6,811,536).

The physiological measurement that forms the basis of Applicant's invention is skin surface vibrations and motions measured using low-power microwave energy. Isolation of the frequency ranges related to the (1) cardiac cycle (heart period, heart frequency, heart rate, etc.), the measurement of the systole time interval (heart valve events within a single heart period, related but physically distinct from the electrocardiography Q-T time interval and the time interval between the "ba-bum" of a single heart beat), and the respiration cycle (respiration rate) is novel.

Meyer's preferred physiological measurement is based on intracardial impedance measurements which are used to measure the cardiac cycle (heart period) from which heart rate variability is evaluated. Sun et al. prefer to use electrocardiography or sphygmography (arterial pressure recorded as a function of time) which, again, is used for heart rate variability measurements. The difference between the cited references and Applicant's

invention relative to the fundamental physiological measurement is, therefore, that in the case of Applicant's invention microwave skin surface monitoring is used to measure the time interval between heart beats, valve events within a heart beat, and respiration events whereas Meyer and Sun et al. use established methods to measure the time interval between heart beats only.

Once the three physiological measures are isolated in the frequency domain, the heart rate information is subjected to established or easily derivable forms of established heart rate variability measures relating to, what is established in the literature as, the low and high frequency powers (normalized or not). In the literature it is common to further subdivide the low frequency region (the very low frequency, the ultra low frequency, etc.) but there has been found to be little value in this exercise as the data is too easily subject to non-physiological interferences using the microwave sensor.

In contrast to the limited value of lower frequency data using the microwave sensor, Applicant has found that the region above 0.4 Hz contains important information that has not been recognized in the prior art. Applicant, therefore, defined the frequency range 0.4 – 1.0 Hz as the "very high frequency or VHF" region. This region corresponds to beat-to-beat variability which is higher in frequency and distinct from high frequency (HF) variability (0.15 – 0.4 Hz). The HF heart rate variability is known in the open literature to be coupled to the respiration rate (i.e., the frequency of the HF band corresponds with the respiration rate of the subject). The VHF and HF frequency regions, therefore, have different underlying neurophysiological origins. While Applicant has observed data presented in the literature that shows power (bands) at frequencies > 0.4 Hz, it is ignored. Data that Applicant has collected indicates that this VHF data is physiologically important and, therefore, represents a novel claim.

The frequency ranges in Applicant's application are defined relative to human subjects only. Animal subjects possess different heart rates, respiration rates, and heart rate variability parameters. In rats, for example, heart rate and respiration rate are higher than in

humans. Heart rate variability parameters also shift toward higher frequencies in rats. Consequently, the defined LF and HF regions are shifted in frequency to accommodate this physiological difference. This is well established in the literature. Therefore, the Sun et al. reference for higher frequency measurements when monitoring Sprague-Dawley rats is not a reference to the monitoring of what Applicant has defined as the VHF region, but rather to the intrinsic physiology difference of the rat relative to humans. Sun et al. do not indicate a recognition that they have identified heart rate variability information at higher frequency than the respiration frequency (i.e., the HF frequency) and, therefore, Sun et al. does not disclose what is claimed related to VHF in Applicant's invention.

During the course of investigation, Applicant found that data processed using established heart rate variability measures with the microwave sensor were sensitive to interferences at frequencies lower than the LF band that complicated interpretation of the results generated. To simplify the results, the data was subject to differentiation, i.e., the difference between adjacent heart beats was used for heart rate variability analysis rather than the heart period itself. This processing step dramatically suppresses low frequency interferences (i.e., it acts as a high pass filter). Suppression of the low frequency interferences was the purpose of the differential analysis, for which it was successful. However, the differential analysis step had the benefit of enhancing the VHF signal strength which is the true origin of Applicant's realization and recognition of the importance of this frequency range.

The differential analysis step is not an established process or recognized as valuable in analysis of heart rate variability in the prior art. In fact, the differential analysis step's very nature suppresses low frequency signals that are believed to be of value to some using other methods of physiological monitoring. As a consequence, investigators have not yet realized the value in differential analysis. Additionally, Applicant believes that the differential analysis method will prove to be useful using sensor technologies other than the microwave sensor including those that are stable in laboratory environments but that are subject to low frequency interferences when used in "noisy" environments. Therefore,

Applicant believes that the differential analysis processing step is novel and a significant contribution to the measurement and interpretation of heart rate variability. Applicant's invention goes further to apply these same concepts to respiration and heart valve event variability analyses which are also believed to be novel.

Acquisition of heart period, heart valve event timing, and respiration frequency using a single skin surface vibration/motion sensor, isolating the physiological measurement (heart rate, heart valve event, and respiration), subjecting each to differential variability analysis, and recognizing and including the VHF region for heart rate variability and differential heart rate variability each represent novel aspects of Applicant's invention relative to Meyer and Sun et al. Therefore, the combination of Meyer and Sun et al. cannot render obvious claims 1-47.

D. **Conclusion:**

Applicant respectfully requests that a timely Notice of Allowance be issued in this case for claims 1-47.

THE JOHNS HOPKINS UNIVERSITY
Applied Physics Laboratory

By Francis A. Cooch
Francis A. Cooch
Reg. No. 31,495
Tel.: (240) 228-5640

FAC/mmlb